15. The composition of claim 2, wherein the aqueous formulation is sufficiently polar to support [MLV] multilamellar vesicle formation

REMARKS

This is in response to the Official Action mailed January 2, 2002 for the above-captioned application. Reconsideration and further examination are respectfully requested.

Applicants have amended claims 5 and 16 in view of the Examiner's objection to the abbreviations.

Claims 1-8 and 9-14 stand rejected under 35 USC § 102(b) as anticipated by US Patent No. 5,643,899 of Elias et al, and claims 9-13, 20 and 21 were rejected as anticipated by or obvious over Elias. The Examiner asserts that the reference discloses compositions containing all of the recited components, and that the structural characteristics recited in the claims, namely that the lipids are in a non-crystalline phase lamellar array and adopt a crystalline lamellar phase when applied to the skin are inherent in the compositions of the reference. Applicants respectfully traverse this rejection.

While the Examiner is correct that the anticipation may be established where the limitations of the claim are inherently present in a prior composition, there are substantial limitations on the application of inherency. Specifically, inherency requires that any unstated elements be a necessary consequence of those which are stated. "Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *Mehl/Biophile International Corp. v. Milgraum*, 52 USPQ2d 1303 (Fed. Cir. 1999). Here the Examiner has taken the position that because the reference recite some of the same component lipids, that it follows that the compositions must have the recited properties. Applicants submit that this conclusion is both legally insufficient and scientifically incorrect.

As a first matter, it is pointed out that claim 1 specifies that the formulation is an **aqueous** formulation. As shown in Example 4, this is an important distinction functionally, since the same mixture of lipids formulated in propylene glycol and ethanol is less effective.

Thus, the Examiner's basic premise that having the same lipids is sufficient to establish that the composition will have the same properties is flawed.

Furthermore, Applicants point out that the Elias patent (Example 1) formulates its lipids in propylene glycol and ethanol, not as an aqueous formulation or uses a detergent such as such as sodium lauryl sulfate to form an emulsion. The Examiner has not specified which of these two formulation types she asserts would inherently have the properties of the claimed invention The first of these formulation types plainly does not anticipate claim 1 or the claims dependent thereon because they are not aqueous formulations. Moreover, the physical characteristics of emulsions are entirely different from those claimed by definition: emulsions are not lamellar phases. While Applicants appreciate that the Examiner may shift the burden of providing laboratory proof that the compositions are in fact different, it is respectfully submitted that there is an initial burden to present a reasoned argument that they might in fact be the same. Here, the obvious lack of an organized lamellar structure in an emulsion, and the absence of anything in the art to suggest that incorporation of lipids into an emulsion would undergo a phase transition on the skin surface to form a crystalline lamellar phase mandates that the Examiner provide some reasons why one of these species or the other might reasonably be deemed to meet the limitations of the claims through inherency before testing by Applicants is required.

The Examiner also rejected claims 1-3, 6-9 and 14-21 under 35 USC § 102(e) as anticipated by US Patent No. 5,916,578 of Kawada et al. Again the Examiner relies on an inherency argument based on similarities in composition to support the contention that Kawada's compositions are non-crystalline phase lamellar arrays that adopt a crystalline lamellar phase when applied to the skin. Applicants point out, however, that Kawada et al. provide data to show that their liquid crystals do ***not*** crystallize (col. 14, lines 18-19; column 13, lines 51-58). Thus, the compositions of Kawada are lamellar liquid crystals that do ***not*** crystallize, whereas the claimed invention is directed to non-crystalline phase lamellar lipid arrays (including but not limited to lamellar liquid crystals) that ***do*** undergo a phase transition to a crystalline lamellar phase. Thus, Applicants submit that Kawada does not anticipate the present claims.

Claims 4 and 5 were rejected as obvious over the Kawada patent. Applicants submit that this rejection suffers from the same deficiencies as the anticipation rejection. Thus, these claims are allowable.

In view of the foregoing, Applicants submit that all claims are in form for allowance. Applicants note that in the Office Action the Examiner has characterized the art. Because the foregoing arguments are believed to be sufficient to overcome the rejections, these characterizations are not addressed herein in detail. This should not be taken as a concession of the accuracy of any of the Examiner's characterization's however. In particular, it is noted that the excerpt from the "Concise Encyclopedia of Chemistry" to which the Examiner refers relates to a specific lipid formulation which is not the same as the formulations of the references. Thus a person skilled in the art would not understand this excerpt to teach anything about the type or size of liposomes which would form from the compositions of the primary references. Furthermore, with respect to Abraham et al., this reference does teach that under certain conditions, an aqueous suspension of stratum corneum lipids may form unilamellar liposomes, and that unilamellar liposomes imply a lamellar liquid crystal (L_α) lipid organization. However, it is not suggested from this paper that such liposomes would adopt a different lipid organization (and in particular a crystalline lamellar phase) when applied to the skin, and indeed these authors provided data in subsequent publications (Abraham et al., 1991, 1992) that their preparations showed no evidence for a crystalline lamellar phase. Indeed, they state in a subsequent review (Abraham et al., 1997, at pg. 183)[1]: "...our results suggest that the SC lipid mixtures exhibit considerable fluidity near the headgroup regions, even at 25°C, and are not in the rigid crystalline state".

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[1] Abraham W, Downing DT (1991) Deuterium NMR investigation of polymorphism in stratum corneum lipids. Biochimica et Biophysica Act 1068, 189. Abraham W, Downing DT (1992) Lamellar structures formed by stratum corneum lipids in vitro: A deuterium NMR study. Pharmaceutical Research 9, 1415. Abraham W, Kitson N, Bloom M, Thewalt JL. Investigation of membrane structure and dynamics by deuterium NMR: Application to the stratum corneum. In "Mechanism of Transdermal Drug Delivery" (RO Potts and RH Guy, eds.) Marcel Dekker, New York, Basel, Hong Kong. Pg. 163-198, 1997.

For these reasons, and in view of the above amendments, this application is now considered to be in condition for allowance and such action is earnestly solicited.

Applicants acknowledge that their election in response to the restriction requirement was without traverse. Since the elected claims are believed to be in form for allowance, however, the Examiner is again urged to consider recombining the claims consistent with the practice as set forth in MPEP § 821.04.

Respectfully Submitted,

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MARKED UP COPY OF AMENDMENTS

In the claims

6. The composition of claim 2, wherein said aqueous formulation of lipids consists of [MLV] multilamellar vesicle or [LUV] large unilamellar vesicle liposomes or a mixture thereof.

15. The composition of claim 2, wherein the aqueous formulation is sufficiently polar to support [MLV] multilamellar vesicle formation